REMARKS

Claims 16-36 are pending in the present application.

Applicants would like to thank Examiner Steadman for the helpful suggestions to address and overcome the objection to the specification; the objection of Claims 22-26 under 37 C.F.R. §1.75; the objection of Claim 30; and the rejection of Claims 11-15, 17, and 22-36 under 35 U.S.C. §112, second paragraph. Applicants have canceled Claims 11-15 and have amended the specification and the claims in accordance with the Examiner's suggestions. As such, the aforementioned objections and rejection are believed to be obviated by amendment. Withdrawal of these objections and grounds of rejection is requested.

The rejection of Claims 11, 12, 14, 15, 18-23, 25, 26, 28-30, and 32-36 under 35 U.S.C. § 112, first paragraph ("written description") is traversed.

The Office has alleged that the specification fails to provide an adequate number of representative species to support the genus provided in the present claims (paper number 18, page 4). Applicants respectfully disagree.

Applicants direct the Examiner's attention to MPEP § 2163.02:

> An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

The Office asserts that "the specification fails to provide a sufficient description of the claimed genus of Escherichia bacteria as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus" (paper number 18, page 5). Applicants, once again, disagree with the Office and specifically refer the Examiner pages 14-17 of the present application. Contrary to the Office's assertion, this section provides an explicit description of the amino acid sequences of the protein, examples of DNA molecules encoding the protein and methods for increasing or

enhancing the activity of the protein, for example, through amplification of copy number and promoter substitution. The specification refers the artisan to references, such as Berg, D.E. and Berg, C.M., Bio/Technol., 1, 417 (1983), for a method for increasing the copy number by introduction of a plasmid, phage, or transposon. In addition, the specification also lists examples of suitable multicopy vectors (see page 16, lines 7-11) for use in the present invention.

Therefore, the present claims do clearly allow the skilled artisan to recognize what has been invented and what is claimed is adequately described in the specification within the meaning of 35 U.S.C. § 112, first paragraph. Accordingly, withdrawal of this ground of rejection is requested.

The rejection of Claims 11, 12, 14, 15, 18-23, 25, 26, 28-30, and 32-36 under 35 U.S.C. § 112, first paragraph ("enablement") is traversed.

The Office has taken the position that while the specification is enabled for bacterium transformed with the polynucleotide of SEQ ID NO:3 or SEQ ID NOS:1 and 3, the specification does not enable one of skill in the art to make and/or use the invention as claimed (page 6-7 of the Office Action, Paper No. 18). Applicants respectfully disagree.

The Office states: "the claims are not so limited to the methods of bacterial modification to increase protein activity as stated in applicants' argument... the scope of the claims is so broad as to encompass an Escherichia bacterium modified by any method and having any modification to increase protein activity" (paper number 18, page 8). Applicants agree that any Escherichia bacterium modified by any method and having any modification to increase protein activity is within the scope of the present claims, provided that increased activity is correlated with the expression of the claims protein and/or nucleic acid sequences. However, this scope is not too broad and is well within the purview of the skilled artisan.

In fact, MPEP § 2164.01 states:

> "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."

Applicants submit that one of skill in the art could obtain and use bacterium having increased protein activity, based on the disclosure provided in the specification, without undue experimentation, especially when the disclosure is augmented with the information known in the art. The specification discloses that increasing expression of the DNA coding for RhtB or RhtC yields an increased activity in the bacterium expressing the DNA thereby increasing L-homoserine or L-threonine resistance (see page 6, line 22 to page 7, line 5). Therefore, the skilled artisan could screen or isolate other bacterium expressing the protein (comprising SEQ ID NO:4) by determining the resistance properties to L-homoserine or L-threonine (see page 7, lines 7-18: "L-threonine resistance means" and "L-homoserine resistance means"); and/or amino acid production (see pages 21-22 "Method for producing an amino acid").

Moreover, MPEP §2164.05(a) states:

> "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public... The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date."

Therefore, the Office's allegation, that "the claims are not so limited to the methods of bacterial modification to increase protein activity as stated in applicants' argument" (see above), is of no moment. In fact, MPEP §2164.05(a) as stated in "the specification... preferably omits that which is well-known to those skilled and already available to the public." Therefore, the failure to state each any every possible method by which the proteins' activities are increased, in and of itself, is not sufficient to support an enablement rejection.

Further, MPEP §2164.04 states:

> "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

At pages 8-23, the Applicants fully describe appropriate methods of isolating, cloning, transforming bacteria, and culturing bacteria harboring the claimed sequences. Moreover, on pages 24-25, the Applicants provide a detailed example showing how to clone the claimed sequences. On pages 25-26, Applicants provide a screening method to identify bacteria containing viable clones. And, on pages 27-36, Applicants have provided examples demonstrating the operability of the present invention.

The Office chooses not to recognize that the present invention is fully enabled, despite satisfying each of the above criteria, and asserts: "The amount of experimentation required to isolate and/or screen for all Escherichia bacteria having any modification by any method that results in an increased protein activity of SEQ ID NO:4 or SEQ ID NOs:2 and 4 would clearly constitute undue experimentation" (paper number 18, page 8). However, Applicants submit that the "amount of experimentation" standard applied by the Office is overly restrictive and can not find support in case law or the MPEP.

In fact, MPEP §2164.06 states:

> "... quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.' "

Applicants submit that, in view of the guidance proffered by the present specification, screening bacteria modified by method resulting in a modification that increases protein activity would require nothing more than routine skill in the art. Again, Applicants point to page 6, line 22 to page 7, line 5 of the specification, which discloses that increasing expression of the DNA coding for RhtB or RhtC yields an increased activity in the bacterium expressing the DNA thereby increasing L-homoserine or L-threonine resistance. Accordingly, whether a modification falls within or without the present claims would require nothing more than assessing L-homoserine or L-threonine resistance.

Therefore, the present claims are deemed to be fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

Applicants submit that the application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

Norman F. Oblon
Attorney of Record
Registration No. 24,618

Vincent K. Shier, Ph.D.
Registration No. 50,552

22850

(703) 413-3000
Fax No.: (703)413-2220
NFO:VKS

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IN THE SPECIFICATION

Please amend the specification as follows:

Page 1, line 1, replace in its entirety with:

--[NOVEL GENE AND METHOD FOR PRODUCING L-AMINO ACIDS] ESCHERICHIA BACTERIUM EXPRESSING POLYPEPTIDES IMPARTING THREONINE- AND HOMOSERINE- RESISTANCE--.

IN THE CLAIMS

Cancel Claims 11-15.

Please amend the claims as follows:

18. (Amended) A method of producing an amino acid, comprising:

cultivating the bacterium as defined in claim [11] 22, which has an ability to produce the amino acid, in a culture medium, to produce and accumulate the amino acid in the medium, and

recovering the amino acid from the medium.

24. (Amended) The bacterium according to claim 22, wherein said bacterium is modified to increase an activity of the protein which makes the bacterium harboring the protein L-threonine-resistant in comparison to a wild-type *Escherichia* bacterium by transformation of said bacterium with DNA coding for the protein, which comprises the amino acid sequence of SEQ ID NO: 4.

27. (Amended) The bacterium according to claim [11] 22, wherein said bacterium is modified to increase an activity of the protein which makes the bacterium harboring the protein L-threonine-resistant by enhancing expression of a gene coding for the protein which comprises the amino acid sequence of SEQ ID NO: 4 in comparison to expression by a wild-type *Escherichia* bacterium.

28. (Amended) The bacterium according to claim [12] 23, wherein said bacterium is modified to increase an activity of the protein which makes the bacterium harboring the protein L-threonine-resistant by enhancing expression of a gene coding for the protein which comprises the amino acid sequence of SEQ ID NO: 4 in comparison to expression by a wild-type *Escherichia* bacterium.

29. (Amended) The bacterium according to claim [12] 23, wherein said bacterium is modified to increase an activity of the protein which makes the bacterium harboring the protein L-homoserine-resistant by enhancing expression of a gene coding for the protein which comprises the amino acid sequence of SEQ ID NO: 2 in comparison to expression by a wild-type *Escherichia* bacterium.

30. (Amended) An isolated bacterium belonging to the genus *Escherichia*, wherein said bacterium is modified to increase an activity of a protein which makes the bacterium harboring the protein L-threonine-resistant in comparison to a wild-type *Escherichia* bacterium, and wherein the protein is encoded by a DNA which is defined in the following (a) or (b):

(a) a DNA which comprises the nucleotide sequence of nucleotide numbers 187 to 804 in SEQ ID NO: 3; or

(b) a DNA which [is] hybridizes to nucleotides 187 to 804 of SEQ ID NO: 3 under a stringent condition, wherein the stringent condition is a condition in which washing is performed at 60°C, and at a salt concentration corresponding to 1 x SSC and 0.1% SDS.

32. (Amended) The bacterium according to claim 31, wherein said bacterium is further modified to increase an activity of a protein which makes the bacterium harboring the protein L-homoserine-resistant in comparison to a wild-type *Escherichia* bacterium, and which comprises the amino acid sequence shown in SEQ ID NO: 2.